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HPV genotypes typed with real-time PCR in an Amazonian region of Ecuador

Genotipos de VPH tipificados con PCR en tiempo real en una región amazónica del Ecuador

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ABSTRACT

The objective of this study was to characterize the most frequent HPV genotypes in patients seen at a clinical laboratory in the province of Napo, Ecuador, between October 2022 and December 2024. A descriptive, cross-sectional, retrospective study of HPV genotyping results using real-time PCR was conducted. Using non-probabilistic convenience sampling, results were obtained from 192 patients of both sexes residing in the province. The predominant age group was 28-33 years old, female. There were no statistically significant differences between the ages of women and men. Molecular testing showed positive results for HPV (≥1 genotype) in 40.6% of the patients. The three most common genotypes were: HPV 68 (25.6%); HPV 16 (23.1%); HPV 51 (21.8%). HPV 68 was also the genotype with the highest relative frequency and distribution in the PAP test results analyzed. The presence of several high-risk genotypes in all Pap test categories underscores the complexity of HPV epidemiology and highlights the importance of genotypic typing using molecular techniques for adequate risk stratification and clinical decision-making.

Keywords: HPV, human papillomavirus genotypes, cervical cancer, PCR.

RESUMEN

El objetivo de este trabajo fue caracterizar los genotipos de VPH más frecuentes en pacientes atendidos en un laboratorio clínico de la provincia de Napo, Ecuador, entre octubre de 2022 y diciembre de 2024. Se realizó un estudio descriptivo, transversal y retrospectivo de resultados de genotipificación de VPH mediante PCR en tiempo real. Mediante un muestreo no probabilístico por conveniencia, se obtuvieron resultados de 192 pacientes de ambos sexos, residentes de la provincia. Predominó el grupo etario de 28-33 años, del sexo femenino. No hubo diferencias estadísticamente significativas entre las edades de mujeres y hombres. Las pruebas moleculares fueron positivas para VPH (≥1 genotipo) en el 40,6% de los pacientes. Los tres genotipos más frecuentes fueron: VPH 68 (25,6 %); VPH 16 (23,1 %) y VPH 51 (21,8 %). El VPH 68 también resultó ser el genotipo con mayor frecuencia relativa y distribución en los resultados del PAP-Test analizados. La presencia de varios genotipos de alto riesgo en todas las categorías del PAP-Test subraya la complejidad de la epidemiología del VPH y destaca la importancia de la genotipificación mediante técnicas moleculares para una adecuada estratificación del riesgo y la toma de decisiones clínicas.

Palabras clave: VPH, genotipos del virus del papiloma humano, cáncer cervicouterino, PCR.

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INTRODUCTION

Human papillomavirus (HPV) is the name given to a group of 200 related viruses that make up the Papillomaviridae family. These non-enveloped viruses have a protein coat or capsid made up of smaller protein units or capsomers, which are repetitive structures that together form a small structure, protecting the viral genetic material, in this case, DNA. HPVs have a replication cycle depending on epithelial differentiation, since their initial infection in stem cells occurs by microscopic rupture of the epithelium (Mogrovejo et al., 2024).

Women can be infected by more than one type of HPV at the same time, and approximately 90% of sexually active men have an infection during their lifetime. The symptoms only appear when the infection, instead of disappearing, persists and progresses, and gives rise to skin lesions on the extremities or in the genital area (genital warts or condylomas). In 90% of cases, the immune system eliminates the infection on its own; however, a persistent infection can progress to precancerous lesions due to high-risk types that can cause cancer of the cervix, vulva, vagina, mouth/throat, penis, and anus. The main prevention method is inoculation through the vaccine that protects before contact, and in addition to vaccination, screening is applied for an early diagnosis and therapeutic approach with a better prognosis. Its presence is common in the population; however, immunocompromised people are those most predisposed to contagion (World Health Organization [WHO], 2024).

Cervical cancer is a global public health problem that primarily affects low- and middle-income countries. According to estimates from the International Agency for Research on Cancer (IARC/WHO) GLOBOCAN project (Ervik et al., 2026), approximately 662,301 new cases of cervical cancer were diagnosed worldwide in 2022, with 348,874 attributable deaths. to this disease, which makes it one of the most frequent and lethal neoplasms among women globally.

In Latin America and the Caribbean, the burden of this disease is also significant: around 63,171 new cases and 33,514 deaths from this cancer were estimated, which represents around 9% of cases and deaths worldwide. Furthermore, data from the Global Cancer Observatory (Ervik et al., 2026) indicate that, in the Americas region, more than 78,000 women were diagnosed and more than 40,000 died from this cancer in 2022, with considerably higher mortality rates in Latin America than in North America, reflecting inequalities in prevention, detection, and treatment

services. In Ecuador, cervical cancer appears among the main cancers in women, with 1,792 new cases and 939 deaths; the 5-year prevalence is approximately 5,456 cases (Ervik et al., 2026). Currently, mortality has decreased, mainly in developed countries, due to the application of timely detection programs through cytological studies available to a greater number of women (Mogrovejo et al., 2024).

Developed in the 1940s, the PAP-Test reduced cervical cancer incidence and mortality as a population screening strategy (Pangarkar, 2022). Richard and Barron (1969) described its cytological progression from intraepithelial neoplasia (CIN I to CIN III and carcinoma *in situ*), until invasive cancer. The Bethesda System, created in 1988 by the National Cancer Institute (NCI) to standardize reporting, has been periodically updated and endorsed by WHO and the American Society of Colposcopy and Cervical Pathology (ASCCP). Although cytology has high specificity for immediate risk, its lower sensitivity and negative predictive value compared to HPV molecular tests limit long-term risk prediction (Perkins et al., 2020). Since the 2000s, qPCR has become a fundamental screening and risk-stratification tool, complementing and sometimes surpassing conventional cytology (WHO, 2021).

The PAP test and cervical brushing qPCR are screening tests, but for a definitive diagnosis, a colposcopy (visual inspection with 3-5% acetic acid to observe areas compatible with precancerous lesions), biopsy, and/or endocervical scraping must be performed (Tests for cervical cancer, n.d.). Molecular techniques are indispensable for the early detection of high-risk genotype infections, which have direct implications for the prevention of precancerous cervical lesions and cancer. However, their high cost is a limiting factor in reducing mortality rates (Estrada et al., 2018). Lineros-Hurtado et al. (2020), in a study in Uruguay, indicated that molecular testing followed by cytology showed greater sensitivity for detecting lesions and that identifying high-risk genotypes benefits the selection of women who should be referred for colposcopy.

Regarding the genotypes detected by qPCR, according to a 2023 update from the NCI, which coincides with the findings of the IARC/WHO (Joshi et al., 2023), there are twelve high-risk HPV genotypes for various types of cancer: 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, and 59, with the first two causing 70% of cervical cancer cases globally (Lazcano-Ponce et al., 2001; Vives et al., 2020). However, the most frequent genotypes globally are not those that predominate in several Latin American and Caribbean countries (Aguilar et al., 2024). In Ecuador, a 2006 study

found the following HPV genotypes: 6, 11, 31, 40, 51, 52, 53, 59, and 68, and that 80% of patients showed infection with more than one HPV genotype (Rodríguez et al., 2006).

Studies in coastal and northwestern Ecuador report HPV 16 and 58 as dominant genotypes and multiple pregnancies as a risk factor (Bedoya-Pilozo et al., 2018; de Los Ángeles Bayas-Rea et al., 2024). Similarly, HPV 31 was most frequent in indigenous women from Cañar, linking infection to sociodemographic factors (Carrión et al., 2019). Although Ecuador's early detection program recommends PAP tests from sexual initiation, national coverage was only 58.8% in 2018 due to promotion deficits, result delays, and specialist shortages (Herrera et al., 2021).

Given that persistent infection with high-risk HPV is the cause of cervical cancer, the identification of circulating genotypes using molecular methods such as qPCR provides evidence for the implementation of early detection and prevention programs for cervical cancer. In this context, it is relevant to characterize the most frequent HPV genotypes in patients seen at a clinical laboratory in the province of Napo, Ecuador, between October 2022 and December 2024, to generate local evidence that contributes to optimizing screening, guiding prevention strategies, and supporting decision-making in public health and clinical practice.

METHODOLOGY

A descriptive, cross-sectional, and retrospective study was conducted on HPV genotyping results from patients who visited a clinical laboratory in the Tena canton of Napo province, Ecuador, between October 2022 and December 2024. The analysis was performed using anonymized databases from the LABTENA S.A.S. laboratory, without access to or manipulation of biological samples. Viral DNA detection results obtained from cervical and urethral samples using qPCR were included.

The study population consisted of all HPV genotyping records obtained by qPCR from individuals seen at the laboratory during the study period. A non-probability convenience sample of 192 patients of both sexes, residing in Napo province, was selected. To avoid duplicate observations, only one record per patient was considered, selecting the first available result from the analysis period. Only records containing demographic variables (age and sex) and analytical variables (HPV genotypes) in the database were included.

The qPCR results were obtained using the Human Papillomavirus (HPV) DNA Diagnostic

Kit (23 Genotypes - PCR - Fluorescence Probe) from SANSURE BIOTECH. This kit is used for the qualitative in vitro detection of HPV types 6, 11, 16, 18, 26, 31, 33, 35, 39, 42, 43, 45, 51, 52, 53, 56, 58, 59, 66, 68, 73, 81, and 82 in exfoliated cervical cells. HPV positivity was defined as the detection of at least one genotype by qPCR (HPV+/GEN+), and the overall and genotype-specific prevalence (n, %) was estimated, as well as the number of coinfections based on the positive genotype count.

The results of Pap smears or cervical cytology tests (PAP tests) were also collected from patients who underwent this test within the sample. The findings were classified according to the Bethesda System into the following categories: negative for intraepithelial lesion or malignancy (NLIM), atypical squamous cells of undetermined significance (ASC-US), high-grade squamous lesion including severe dysplasia (CIN III), low-grade squamous intraepithelial lesion including mild dysplasia (CIN I), and moderate cervicovaginal inflammatory process (cervicovaginitis).

The categorical variables sex, sample type, and cytological categories were summarized using absolute and relative frequencies. Normality was assessed using the Kolmogorov-Smirnov test, and when deviations from normality were observed ($p < 0.01$), age comparisons between sexes were performed using the Mann-Whitney U test. The age variable was grouped using Sturges' rule with $n = 192$, resulting in 9 classes; intervals were constructed, including the minimum and maximum values (years). Spearman's rho coefficient, appropriate for dichotomous variables (presence/absence), was used to assess genotype co-occurrence (coinfection); $p < 0.05$ was considered significant. Statistical analysis was performed using SPSS version 25 software. The collected information was treated with confidentiality and discretion. Approval was received from the Human Research Ethics Committee of the Technical University of Manabí (CEISH-UTM), which in turn has the approval of the Ministry of Public Health (MSP) of Ecuador. The approval code was CEISH-UM-INT_25-07-16_CFFA.

RESULTS AND DISCUSSION

Women, whose samples were obtained by cervical brushing, were more frequent (87.5%) compared to men (12.5%), in whom urethral brushing was used. The mean age in women was 36.25 ± 1.33 years and in men 34.20 ± 2.79 years (Table 1), with no statistically significant difference ($p = 0.182$). Ages ranged from 16 to 70 years (Figure 1), with the highest concentration

of participants in the 28–33 age group (25.5%). From age 51 onward, a progressive decrease in the number of individuals was observed, with little representation in the age groups over 60 years.

Table 1. Distribution of the sample by age and sex

Sex	n	Percentage	Average (Years)	Standard error of the average	Median (Years)	Minimum age (Years)	Maximum age (Years)
Female	168	87.5	36.25	1.33	34	18	70
Male	24	12.5	34.20	2.79	32	16	64

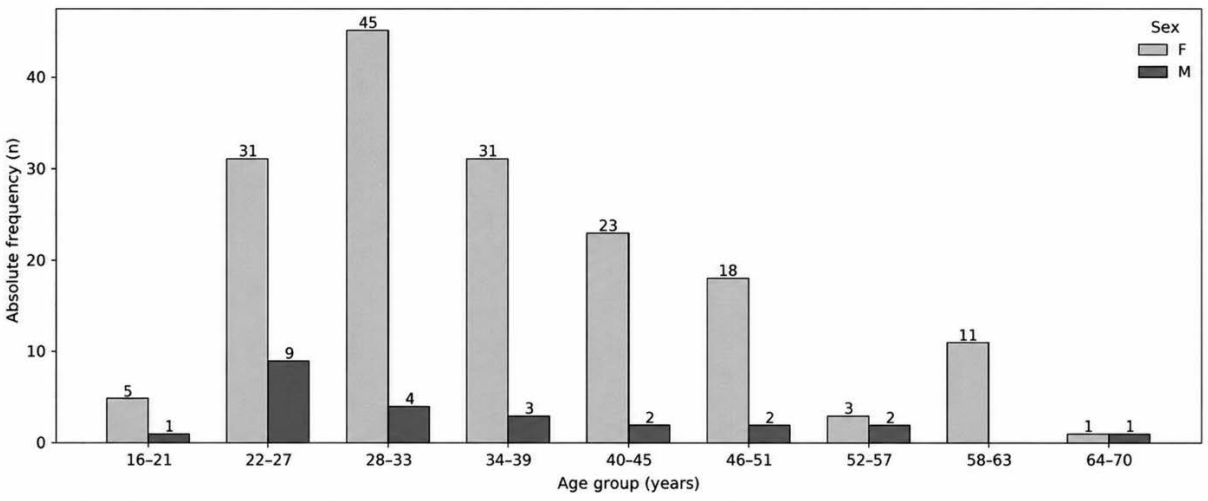

Figure 1. Distribution of the sample according to sex and age group.

The observed age distribution pattern corresponds to global findings showing peaks in infection in young populations and a progressive decrease in older individuals, although with variations between geographic regions and detection methods. Similar age-related prevalence patterns have been described in various populations, where HIV infection tends to be more common in sexually active young adults and decreases in older age groups, which could be related to changes in sexual exposure and acquired immune response over time (de Los Ángeles Bayas-Rea et al., 2024). The progressive decrease in the number of individuals from age 51 onward observed in this study has been previously described in population-based research, which reports lower participation of older adults in screening programs and a reduction in transient infections at advanced ages (Muñoz et al., 2003; Arbyn et al., 2020). However, some studies (Trujillo et al.,

2017; Arrossi, 2019) in contexts with limited access to molecular screening have described a second peak in prevalence among older women, suggesting that age-related patterns may vary according to sociodemographic conditions and healthcare coverage.

The predominance of females and the collection of samples via cervical brushing reflect the historical orientation of cervical cancer prevention programs, which have prioritized screening in women. Globally, it is estimated that approximately 12% of women have HPV infection, with higher prevalence rates in regions such as Latin America, where factors such as social inequality, limited access to screening programs, and variability in vaccination coverage influence the persistence of the infection (WHO, 2024). In this context, the use of sensitive molecular techniques such as qPCR is essential for the detection and accurate characterization of circulating genotypes. This situation has been documented in the literature, which acknowledges that male participation in HPV studies remains limited, despite their role in virus transmission (Garland & Smith, 2010; Vives et al., 2020). The lower male representation and the use of urethral brushing observed in this study are consistent with previous reports from several years ago in Latin American populations (Lazcano-Ponce et al., 2001; Aguilar, 2006).

The absence of statistically significant differences between the ages of women and men coincides with studies indicating that the age of acquisition of the viral infection does not differ substantially between sexes when analyzing general populations (Bosch & de Sanjosé, 2007). However, it has been described that the persistence of the infection and the progression to associated lesions can be modulated by hormonal, immunological, and behavioral factors, particularly in women (de Los Ángeles Bayas-Rea et al., 2024).

Molecular testing was negative in 114 patients (59.4%), and 78 cases (40.6%) were qPCR-positive for HPV (≥1 genotype). HPV genotypes 68, 16, and 51 predominated, followed by 58 and 39, while several genotypes (HPV 33, 35, 73, and 82) were infrequent (≤2 cases), and no positivity was found for HPV 26 and 11 (Figures 2 and 3). Among the genotypes identified in samples infected with a single genotype (n=43) detected by qPCR, the following were found in order of frequency: HPV 68 (9 cases; 11.5%), HPV 51 (6 cases; 7.7%), HPV 39 and 16 (each in 4 cases; 5.1%), HPV 42 and 59 (each in 3 cases; 3.8%), HPV 58, 56, 52, and 31 (each in 2 cases; 2.6%), and HPV 81, 43, 82, 45, 35, and 18 (each in 1 case; 1.3%).

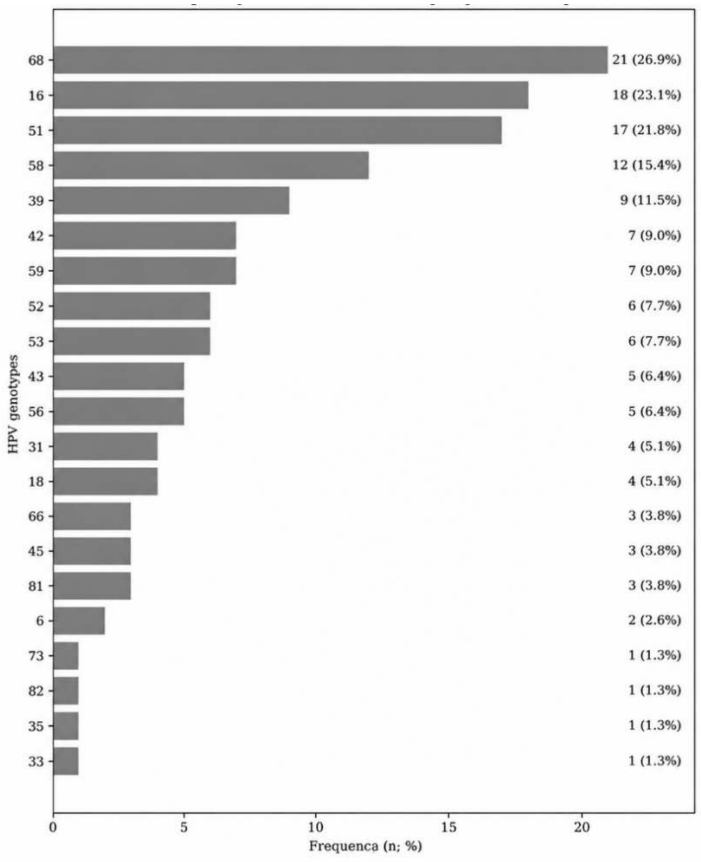

Figure 2. Distribution of HPV genotypes detected by qPCR in the analyzed sample (n=78), expressed as absolute frequency and percentage.

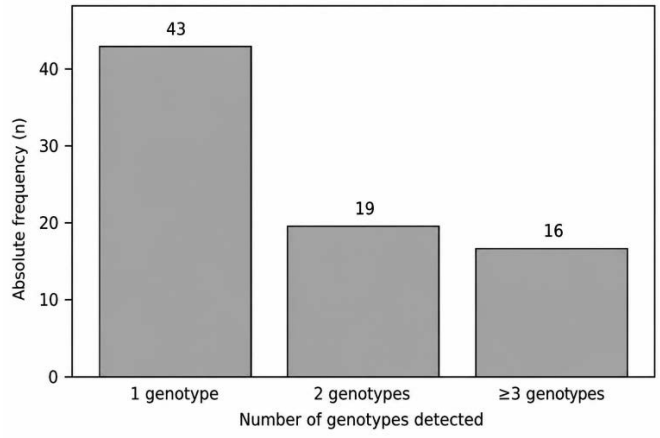

Figure 3. Distribution of the number of HPV genotypes detected per sample. The bars represent the absolute frequency (n) of samples with one, two, or three or more genotypes identified by qPCR.

Among the most frequent exact combinations of two genotypes (n=19), the most frequent were HPV 51+68 and 16+43. HPV 16+68 and HPV 16+51 (each in 2 cases; 2.6%). Among the exact combinations of coinfection with three or more viral genotypes (n=16) detected by qPCR, the co-occurrence of HPV 16+51+68 was observed in two cases (2.6%). In total, coinfections of three different types were observed in 10 cases, four different types in 3 cases, and five different types in 2 cases. Figure 4 shows which pairs most frequently co-occurred in the studied population, regardless of their presence within combinations with three or more genotypes.

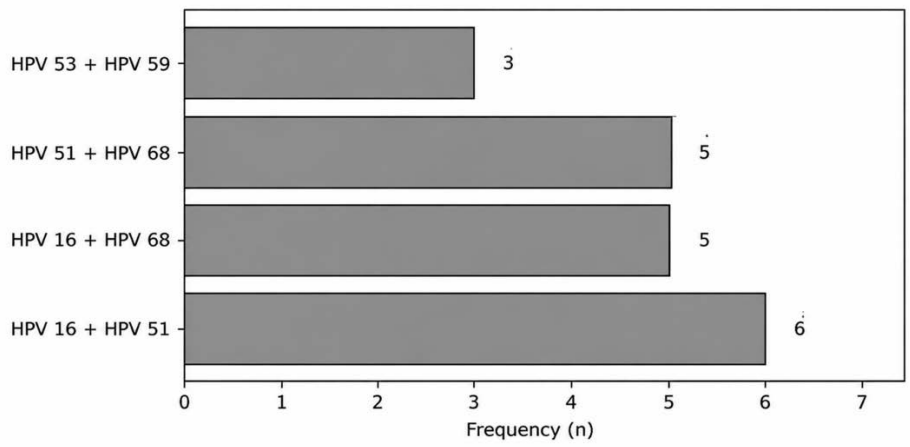

Figure 4. Distribution of the most frequently co-occurring human papillomavirus (HPV) genotype pairs in the studied population, regardless of their presence within combinations with three or more genotypes.

According to Muñoz et al. (2003) in a study that included more than a thousand women from nine countries (including four South American countries), concluded that, in addition to HPV genotypes 16 and 18, types 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82 should be considered carcinogenic or high-risk, and types 26, 53, and 66 should be considered probably carcinogenic. Coinfection has been described by Cassini et al. (2024) and has been associated with high-grade epithelial lesions, but exposure may be primarily determined by the persistence of the highest-risk genotype, and evidence regarding any type of synergy between genotypes is heterogeneous. In some populations, coinfection may be associated with more severe lesions, but it is acknowledged that the results are not conclusive (Jing et al., 2025).

Regarding the higher frequency of the high-risk HPV genotypes 68, 16, 51, 58, and 39 found in this study, alone or coexisting with others, there are some consistencies and discrepancies with other studies. However, it is important to mention that the virus distributions reported in clinical populations support the idea that the prevalence and distribution by genotype vary between studies and between countries, reflecting epidemiological heterogeneity (Mosquera-Yuqui et al., 2025; Osmani, Hörner, et al., 2025; Osmani, Rossiter, et al., 2025). Matches were observed in only two genotypes (HPV 16 and 58) with the five most prevalent genotypes in women with positive results worldwide, which, according to Le et al. (Le et al., 2024) are HPV 16, 18, 31, 58, and 52. Agreements were found with Chinese studies (Liu et al., 2023) that reported HPV 58, 16, 68, and 51 as the most frequent genotypes, and that of Zhou et al. (2009), who described HPV 58, 16, 51, and 39 in their top genotypes.

Correa et al. (2022) described that in Latin America, the most frequent HPV genotypes were 16 and 31, while HPV 52, 58, 33, 18, and 39 were found at frequencies below 13%. Solis-Ponce et al. (2025) described oncogenic HPV types in 35.7% (192/538) of the participants in their study, with HPV 16 and 52 being the most prevalent.

Regarding Ecuador, and according to IARC/WHO (Bruni et al., 2023), local patterns may differ and should be interpreted with a regional focus. The frequency of HPV 16, 58, and 52 is described for cervical cancer. De los Angeles Bayas-Rea et al. (2024) reported that in women of different ethnicities in the rural Northwest, HPV genotypes 58, 16, 68, and 39 were the most common, and explicitly noted that the distribution varies widely and changes according to population/ethnicity. García et al. (2025) in patients of the Society for the Fight Against Cancer (SOLCA) in Guayaquil, describe HPV genotypes 16, 18, and 58 as the most frequent, and describe other high- and probable-high-risk types that were also common, such as HPV 31, 52, 53, and 56. Some studies have shown a high diversity of circulating high-risk oncogenic HPV genotypes in Ecuador, among which HPV 16 and 58 stand out.

While HPV genotypes 16 and 18 continue to be the most relevant worldwide due to their close association with cervical cancer, this study identifies other high-risk oncogenic genotypes that, along with those described in the literature, exhibit significant genotypic diversity in local populations and should be considered in the planning of prevention, screening, and therapeutic approaches to optimize the effectiveness of interventions in specific epidemiological contexts.

It is important to note that regarding the frequency of HPV 16, studies should be conducted in the studied population on variants according to mutations in the E6, E7, and L1 genes (Le et al., 2024; Solis-Ponce et al., 2025). Long-term viral persistence is necessary for malignancy, and HPV has several mechanisms to evade an effective immune response, which can lead to failure to eliminate the infection. The two main viral oncoproteins involved are E6 and E7, which promote cell immortality and, consequently, transformation and carcinogenesis. On the other hand, the L1 gene is fundamental for the early interaction of the capsid with the host cell. The two HPV 16 genetic lineages that cocirculate in the global population and that could represent differences in pathogenicity and epidemiology impacting screening and treatment are the European (A1, A2, A3) and Asian (D1, D2, and D3) lineages. Asian HPV 16 is generally much more aggressive than its European counterpart, leading to the development of precancerous cervical lesions in a much shorter time (Bedoya-Pilozo et al., 2018). An analysis of HPV 16 sublineages in a population from the Peruvian Amazon (Solis-Ponce et al., 2025) revealed a predominance of A1 variants, while viral integration was detected in nine cases, three of which were associated with CIN II lesions. These findings highlighted the urgent need to expand vaccination and implement molecular screening strategies in the Peruvian Amazon.

Ecuador, for its part, is home to a multiethnic society resulting from contact between Indigenous communities, the conquistadors, and enslaved Africans. Ecuadorian mestizos primarily have Native American ancestry (66.1%), with some European admixture (30.0%) and small amounts of African (2.4%) and East Asian (1.5%) genetic ancestry (Nagar et al., 2021). The long-term impact of HPV 16 detection in the Ecuadorian trihybrid population will need to be analyzed to assess whether any polymorphisms promote the development of endocervical lesions or cervical cancer, or whether, on the contrary, these genetic changes could have the opposite effect (Rivera et al., 2018).

Regarding the Pap test, of the 168 women screened, only 79 (47.0%) underwent the test, with the results distributed in Table 2. This low percentage can be attributed, in part, to clinical screening criteria such as gynecological and obstetric history, time elapsed since the last screening, and the presence of symptoms. Screening guidelines recommend specific intervals for cervical cytology, so women with a recent Pap test or outside the prioritized age range may not be retested at the time of the molecular study.

Table 2. Distribution of cytological test (PAP-Test) results in the women studied

Category	n	Percentage
Unrealized	89	53.0
Completed	79	47.0
Total	168	100
Cervicovaginitis	35	44.3
NLIM	28	35.4
NIC III	8	10.1
NIC I	7	8.9
ASC-US	1	1.3
Total	79	100

Other factors may have also played a role, such as patient voluntary consent and/or operational limitations inherent to the healthcare setting, where the HPV test could be performed independently of cervical cytology. In Amazonian and rural contexts, such as the province of Napo, sociocultural factors, geographical barriers, limited access to gynecological services, and the availability of trained personnel may have contributed to lower PAP test coverage, even when women participated in other screening activities, such as HPV molecular testing.

Additionally, within the study, HPV determination by qPCR was performed independently of the Pap test, using samples previously obtained or collected for molecular diagnostic purposes. Finally, it should be noted that the study has an observational design, based on records and routine clinical practices. Therefore, the Pap test coverage reflects the reality of screening in the studied environment and not an intervention designed to administer cytology to all participants. These factors explain why, in this study, a greater number of women have HPV test results, while only a fraction underwent cervical cytology during the same period.

The PAP test remains essential as a complement to diagnosis. Kang et al. (2020) evaluated the usefulness of the Pap smear and HPV tests as diagnostic screening tools in one institution and found that the sensitivity and specificity for detecting high-grade squamous intraepithelial lesions and squamous cell carcinoma were higher for vaginal cytology than for HPV testing. They concluded that the Pap smear was more useful than the HPV test in diagnosing these cervical lesions. Kim et al. (2020), in a published study, demonstrated that combining cytology and HPV testing increased sensitivity and specificity compared to either method alone, and that, therefore, cytology and HPV testing are complementary.

To study the correlation between the different genes, Spearman's rho correlation coefficient was calculated, as well as their significance. The genes with significant correlations are summarized in Table 3. The correlation analysis identified statistically significant positive associations between certain HPV genotypes, highlighting the correlations considered to have a sufficient detection frequency. Moderate positive correlations were identified between GEN18 and GEN73 (ρ=0.490; p<0.001), as well as between GEN53 and GEN59 (ρ=0.414; p<0.001). Additionally, GEN73 showed a consistent association with GEN53 (ρ=0.395; p<0.001), suggesting a pattern of co-occurrence or coinfection between these genotypes. Other correlations, although statistically significant, were excluded due to low detection frequency.

Table 3. Statistical correlation between the different genes detected

Genes		Spearman's rho	p-value	Significance
GEN58	GEN33	0.267	0.018	*
GEN66	GEN45	0.307	0.006	**
GEN59	GEN53	0.414	0.000	***
GEN73	GEN18	0.490	0.000	***
GEN73	GEN53	0.395	0.000	***
GEN6	GEN53	0.258	0.023	*
GEN42	GEN33	0.363	0.001	**
GEN81	GEN18	0.256	0.024	*
GEN73	GEN26	0.363	0.001	**
GEN42	GEN35	0.363	0.001	**

* Significant ($p \leq 0.05$); ** Highly significant ($p \leq 0.01$); *** Highly significant ($p \leq 0.001$).

The positive correlations observed between certain HPV genotypes, while suggesting the presence of non-random patterns of coinfection, particularly among high-risk oncogenic genotypes, could reflect shared exposure, common biological susceptibility, or viral persistence dynamics.

It is important to note that Spearman's rank correlation coefficient does not imply causality, that the correlations were mostly moderate ($\rho \approx 0.25–0.49$), and that the magnitude suggests frequent coexistence, not strong dependence. Furthermore, most genotype pairs did not show a statistically significant correlation, which could indicate that many genotypes circulate independently, that there is no pattern of coinfection, and that coinfection appears selective, not widespread. Overall, the associations could be related to shared mechanisms of viral transmission or persistence; however, due to the cross-sectional design of the study and the exploratory nature

of the correlation analysis, these findings should be interpreted with caution and do not imply a direct causal relationship between the genotypes.

The HPV genotypes most frequently detected by qPCR were predominantly associated with females (Table 4), mainly concentrated in age groups under 49 years, which coincides with the period of greatest sexual activity and risk of viral persistence. HPV 16, followed by genotypes 51 and 68, was the most frequently identified and was observed more often in women with abnormal cytology results, especially low- and high-grade intraepithelial lesions. However, infections with high-risk genotypes were also identified in patients with negative Pap smears, demonstrating the usefulness of qPCR for detecting subclinical infections not evident by cytology.

Table 4. Distribution of positive genotypes by sex

Variable	Sex	n	Percentage
Number of genotypes HPV positive	Female	64	82.1
	Male	14	17.9
	Total	78	100

A decreasing trend in the frequency of HPV detection was observed with increasing age, being highest in women ≤39 years (Figure 5). Genotypes 68, 16, and 51 had the highest detection frequency and a broad distribution across young and middle-aged adults. Genotype 58 was detected exclusively in women and showed sustained presence across various age ranges, while genotype 39 exhibited a more balanced distribution between sexes. Genotypes 42 and 59 showed lower frequencies and limited age dispersion, suggesting a secondary contribution to the overall burden of infection.

Taken together, these patterns reflect a heterogeneous HPV genotypic distribution, consistent with clinical populations as described above, and highlight the utility of molecular screening by qPCR for identifying high-risk genotypes beyond HPV 16 and 18. A recent epidemiological study (Zhu et al., 2025) assessed how the prevalence of high-risk HPV genotypes varies among different age groups and between women and men, finding that the prevalence of high-risk genotypes was significantly higher in adolescents and decreased with age, and that women had higher infection rates with high-risk genotypes than men in virtually all age ranges analyzed ($p < 0.001$). Another recent study in Iran (Mojarrad et al., 2025) also shows a prevalence

and genotypic distribution that varies with age and between sexes, supporting the notion that genotypic distribution is not homogeneous in the general population.

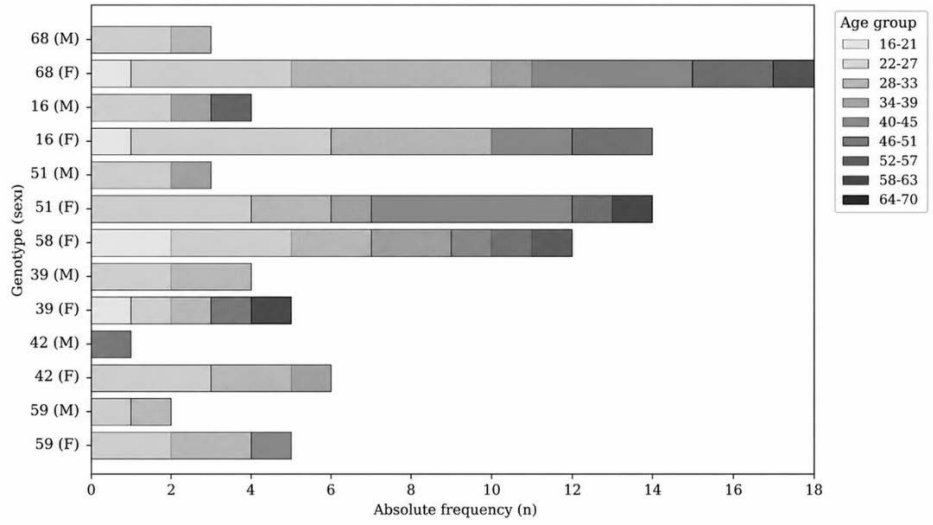

Figure 5. Distribution of the most frequent HPV genotypes detected by qPCR according to sex and age group in the studied population, regardless of their presence alone or in combinations with three or more genotypes.

Of the 79 cases with Pap test results, 53 had all genotypes negative, and 26 had at least one positive HPV genotype. Of these, 15 cases had monoinfection, and 11 had coinfection. In all cases, regardless of the histopathological result, high-risk oncogenic genotypes were identified more frequently, and the most frequent coincided with the overall qPCR detection results: HPV 68, 16, and 51, with multiple coinfections observed. Most detections were associated with abnormal cytology, although some genotypes were also identified in normal cytology (NLIM). In high-grade lesions (CIN III), qPCR was positive in 50% of cases (4/8). Six qPCR-positive cases were identified even with negative Pap tests, indicating subclinical infection.

Figure 6 correlates PAP test cases with HPV genotypes found in positive qPCR results. A heterogeneous distribution of HPV genotypes is evident according to the Papanicolaou cytological categories, considering only cases with a positive PAP test and HPV (n = 26). The intensity of the inverted grayscale coloration reflects the percentage of positivity for each genotype within each cytological category, revealing differential patterns of genotypic presence.

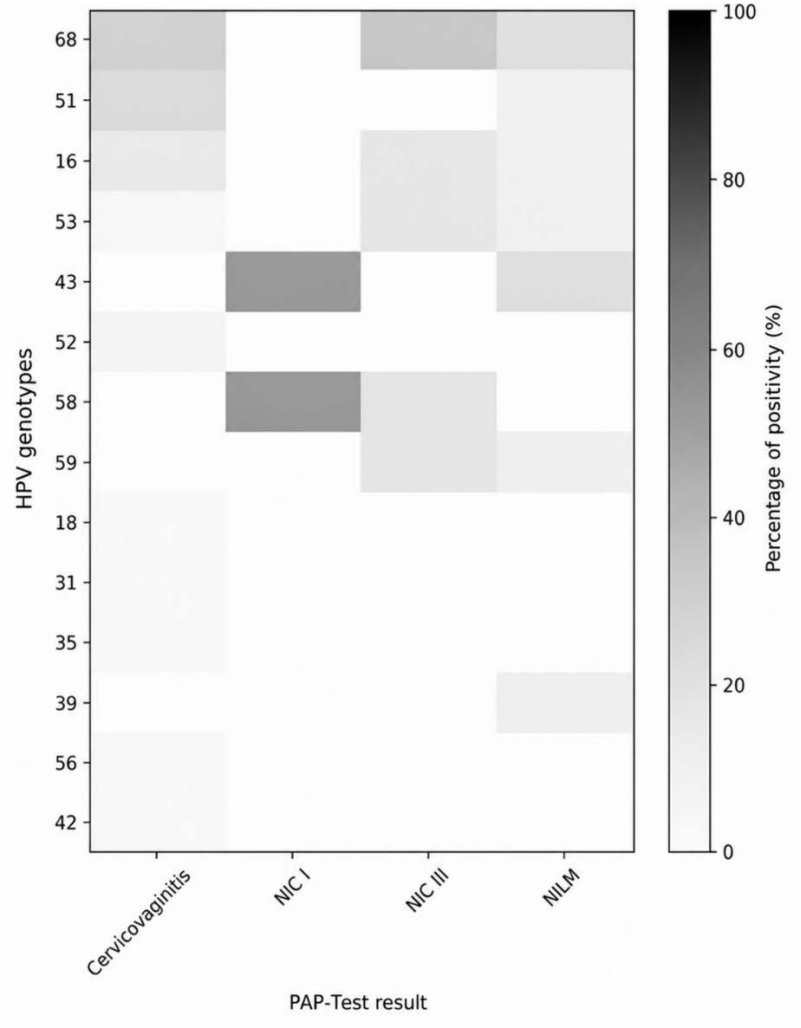

Figure 6. Distribution of HPV genotypes according to Papanicolaou cytological categories. The heat map represents the percentage of positivity for each genotype within each cytological category. NLIM: Negative for intraepithelial lesion or malignancy; ASC-US: Atypical squamous cells of undetermined significance; CIN III: High-grade squamous lesion; CIN I: Low-grade squamous intraepithelial lesion; and Moderate inflammatory: cervicovaginitis.

In the NLIM category, a higher relative frequency of HPV genotypes 68, 51, 43, and 16 is observed, indicating that these genotypes can be detected even in cytologically normal samples. This finding suggests the presence of infections that could be subclinical or transient, consistent with the natural history of HPV, where infection can precede the appearance of cytological abnormalities. In cases of cervicovaginitis, the heat map shows a broader distribution of genotypes,

with HPV 68 standing out as the most frequently occurring genotype, followed by HPV 51, 53, and 16. The coexistence of multiple genotypes in this category supports the association between HPV infection and cervical inflammatory processes, as well as the possibility of coinfections in inflammatory contexts.

In the CIN III category, a marked intensification for HPV 68 is observed, along with the significant presence of HPV 53, 59, and 16, suggesting a higher concentration of high-risk oncogenic genotypes in high-grade intraepithelial lesions. This pattern reinforces the hypothesis that, in addition to the classic HPV 16 and 18 genotypes, other high-risk genotypes, such as HPV 68 and 53, may play an important role in the progression of cervical lesions in this population. The CIN I category shows a concentrated positivity rate primarily for HPV types 58 and 43, reflected by high color intensity, suggesting that these genotypes were present in all cases with low-grade intraepithelial lesions. Although the overall number of cases is limited, this finding points to a possible role for these genotypes in the early stages of cytological abnormalities.

HPV type 68 emerges as the most frequently occurring genotype, with a wide distribution across the different cytological categories of the Pap test, from normal to high-grade lesions. The presence of several high-risk genotypes in all Pap test categories underscores the complexity of HPV epidemiology and highlights the importance of genotyping using molecular techniques for appropriate risk stratification and clinical decision-making.

Low-risk genital HPV types have been primarily associated with genital warts, while high-risk types are frequently associated with invasive cervical cancer. Despite this, there is no consensus on the risk associated with low-frequency HPV genotypes. For these reasons, clear criteria are still needed to classify HPV types into low- and high-risk groups based on molecular epidemiological studies of different populations, providing estimates of risk and oncogenic potential (Muñoz et al., 2003; Le et al., 2024).

It is important to note that in this study, HPV was detected by qPCR in 52 patients who did not undergo Pap testing, highlighting the value of molecular diagnosis independent of cytological screening. On the other hand, high-risk HPV infection is a necessary but not sufficient cause of cervical cancer, since, according to the IARC, most women who contract the infection will not develop cancer. Some cofactors can increase a woman's susceptibility to persistent HPV infection,

which can eventually progress to malignancy. These cofactors, which could not be elucidated in this study due to a lack of patient data, include, according to the literature, infection at a young age, multiple births at a young age, smoking, HIV infection, genital tract infections (*Trichomonas vaginalis*, *Chlamydia trachomatis*, and herpes simplex virus type 2), and immunosuppression. Additionally, persistent infection with high-risk HPV genotypes leads to the development of premalignant squamous epithelial lesions (CIN), which, if not detected and treated promptly, can progress to invasive cervical cancer within 5 to 10 years (Joshi et al., 2023).

Finally, it is worth noting the findings of Garland & Smith (2010) regarding the availability of two prophylactic cervical cancer vaccines based on HPV virus-like particle technology, which have the potential to significantly reduce cervical cancer cases worldwide. However, to be a successful public health tool, it must be applied without restrictions to the appropriate target population, preferably before first sexual intercourse or at least to all young adult women up to age 26. Immunity to HPV is primarily type-specific, so the protection induced by the current generation of vaccines cannot provide complete protection against all oncogenic HPV types. Therefore, it is essential to ensure affordable testing, provide education at all levels, and promote continued adherence to screening programs.

CONCLUSIONS

The analyzed population was predominantly female and young adults, with no significant age differences by sex, although cases decreased after age 51. 40.6% tested positive for HPV (≥1 genotype), with HPV 68, HPV 16, and HPV 51 being the most frequent, in that order. Moderate positive associations were identified between HPV 18 and 73, HPV 53 and 59, and HPV 73 and 53, suggesting coinfection patterns. The frequency of HPV detection decreased with age, with a higher prevalence in women ≤29 years. HPV 68 showed the highest distribution in the Pap test results, followed by HPV 16. The presence of multiple high-risk genotypes in all cytological categories demonstrates the epidemiological complexity of HPV and highlights the need for molecular typing for adequate risk stratification. The findings provide relevant local epidemiological evidence for the Amazon region of Ecuador and reinforce the importance of strengthening prevention strategies, molecular screening, and vaccination adapted to the context, to reduce the burden of infection and its oncogenic consequences.

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CONFLICTS OF INTEREST

The authors declare that they have no conflicts of interest.

AUTHOR CONTRIBUTIONS

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REFERENCES

Aguilar, J. T., Ortiz, J. G., & Vizhñay, M. G. (2024). Genotipos de alto riesgo del Virus del Papiloma Humano en mujeres de América Latina y el Caribe. *Revista Vive*, *7*(21), 788-802. https://doi.org/10.33996/revistavive.v7i21.339

Aguilar, L. V. (2006). Human papillomavirus in men: Comparison of different genital sites. *Sexually Transmitted Infections*, *82*(1), 31-33. https://doi.org/10.1136/sti.2005.015131

Arbyn, M., Weiderpass, E., Bruni, L., Sanjosé, S. de, Saraiya, M., Ferlay, J., & Bray, F. (2020). Estimates of incidence and mortality of cervical cancer in 2018: A worldwide analysis. *The Lancet Global Health*, *8*(2), e191-e203. https://doi.org/10.1016/S2214-109X(19)30482-6

Arrossi, S. (2019). El impacto de la prueba de VPH en los programas de tamizaje en América Latina: El caso de Argentina. *Salud Pública de México*, *61*(1), 86-94. https://doi.org/10.21149/9257

Bedoya-Pilozo, C. H., Medina, L. G., Espinosa, M., Sánchez, M., Parrales, J. V., Molina, D., Ibarra, M. A., Quimis, M., España, K., Párraga, K. E., Cajas, N. V., Orlando, S. A., Robalino, J. A., Chedraui, P., Escobar, S., Loja, R. D., Ramirez, C., Espinoza, J., Sánchez,

S., … Badano, I. (2018). Molecular epidemiology and phylogenetic analysis of human papillomavirus infection in women with cervical lesions and cancer from the coastal region of Ecuador. *Revista Argentina de Microbiologia, 50*(2), 136-146. https://doi.org/10.1016/j.ram.2017.06.004

Bosch, F. X., & Sanjosé, S. de. (2007). The epidemiology of human papillomavirus infection and cervical cancer. *Disease Markers, 23*(4), 213-227. https://doi.org/10.1155/2007/914823

Bruni, L., Albero, G., Serrano, B., Mena, M., Collado, J. J., Gómez, D., Muñoz, J., Bosch, F. X., & de Sanjosé, S. (2023). *Human Papillomavirus and Related Diseases in Ecuador: Summary Report*. ICO/IARC Information Centre on HPV and Cancer (HPV Information Centre). Retrieved December 28, 2025, from https://hpvcentre.net/statistics/reports/ECU.pdf

Carrión, J. I., Soto, Y., Pupo, M., & Loja, R. (2019). Infección por Virus del Papiloma Humano y citología cérvico-vaginal en mujeres indígenas del Cañar, Ecuador. *Bionatura, 4*(3), 934-938. https://doi.org/10.21931/RB/2019.04.03.10

Cassani, C., Dominoni, M., Pasquali, M. F., Gardella, B., & Spinillo, A. (2024). The role of multiple high-risk human papillomavirus infection on the persistence recurrence of high-grade cervical lesions after standard treatment: A systematic review and a meta-analysis. *Acta Obstetricia et Gynecologica Scandinavica, 103*(6), 1028-1035. https://doi.org/10.1111/aogs.14827

Correa, R. M., Baena, A., Valls, J., Colucci, M. C., Mendoza, L., Rol, M., Wiesner, C., Ferrera, A., Fellner, M. D., González, J. V., Basiletti, J. A., Mongelos, P., Peña, M. R. de la, Saino, A., Kasamatsu, E., Velarde, C., Macavilca, N., Martinez, S., Venegas, G., … Group, E. S. (2022). Distribution of human papillomavirus genotypes by severity of cervical lesions in HPV screened positive women from the ESTAMPA study in Latin America. *PLOS ONE, 17*(7), e0272205. https://doi.org/10.1371/journal.pone.0272205

Dalgo, P., Loján, C., Córdova, A., Acurio, K., Arévalo, A. P., & Bobokova, J. (2017). Prevalence of high-risk genotypes of human papillomavirus: Women diagnosed with premalignant and malignant Pap smear tests in Southern Ecuador. *Infectious Diseases in Obstetrics and Gynecology, 2017*, 8572065. https://doi.org/10.1155/2017/8572065

de Los Ángeles Bayas-Rea, R., Ponce, K., Guenther, A., Mosquera, J. D., Armijos, C., Mejía, L., Bustamante, G., & Zapata, S. (2024). Prevalence of human papillomavirus genotypes in

women of different ethnicity from rural northwestern Ecuador. *BMC Global and Public Health, 2*(1), 46. https://doi.org/10.1186/s44263-024-00078-x

Ervik, M., Laversanne, M., Lam, F., Colombet, M., Ferlay, J., Filho, A. M., & Bray, F. (2026). *Global Cancer Observatory: Cancer Today (2024 estimates, version 1.0)*. International Agency for Research on Cancer. Retrieved December 28, 2025, from https://gco.iarc.who.int/media/globocan/factsheets/cancers/23-cervix-uteri-fact-sheet.pdf

Estrada, J. P., & Ulloa, A. (2018). Diagnóstico del virus del papiloma humano en mujeres en edad fértil del área de salud No. 1 de Azogues, Ecuador. *Revista Información Científica, 97*(1), 19-28.

García, G. D., Abdul, F., Beltrán, C. C., Medina, S., & Ruiz, J. C. (2025). High frequency of HPV high-risk preventable genotypes in Ecuadorian women with invasive cervical cancer. *Revista Panamericana de Salud Pública, 48*, e128. https://doi.org/10.26633/RPSP.2024.128

Garland, S. M., & Smith, J. S. (2010). Human papillomavirus vaccines: Current status and future prospects. *Drugs, 70*(9), 1079-1098. https://doi.org/10.2165/10898580-000000000-00000

Herrera, E. M., Salazar, Z. K., Espinosa, L., & Aspiazu, K. A. (2021). Detección oportuna de cáncer cérvico-uterino. *Revista Vive, 3*(9), 264-274. https://doi.org/10.33996/revistavive.v3i9.65

Jing, Y., Chen, J., Lin, F., Huang, X., Liu, Y., Zhao, M., Ye, C., Zhao, L., Liu, X., & Yang, J. (2025). Multiple high-risk human papillomavirus infections exacerbate cervical lesion risk: Epidemiological evidence from Suining, Sichuan. *Virology Journal, 22*(1), 268. https://doi.org/10.1186/s12985-025-02904-6

Joshi, S., Basu, P., & Lucas, E. (2023). *Using HPV tests for cervical cancer screening and managing HPV-positive women – a practical online guide* (IARC CancerBase No. 18). International Agency for Research on Cancer. Retrieved December 28, 2025, from https://screening.iarc.fr/atlasHPV.php

Kang, M., Ha, S. Y., Cho, H. Y., Chung, D. H., Kim, N. R., An, J., Lee, S., Seok, J. Y., & Jeong, J. (2020). Comparison of papanicolaou smear and human papillomavirus (HPV) test as cervical screening tools: Can we rely on HPV test alone as a screening method? An 11-year retrospective experience at a single institution. *Journal of Pathology and Translational Medicine, 54*(1), 112-118. https://doi.org/10.4132/jptm.2019.11.29

Kim, M. S., Lee, E. H., Park, M. I., Lee, J. S., Kim, K., Roh, M. S., & Lee, H. W. (2020). Utility of Human Papillomavirus Testing for Cervical Cancer Screening in Korea. *International Journal of Environmental Research and Public Health, 17*(5), 1726. https://doi.org/10.3390/ijerph17051726

Lazcano-Ponce, E., Herrero, R., Muñoz, N., Hernandez-Avila, M., Salmerón, J., Leyva, A., Meijer, C. J., & Walboomers, J. M. (2001). High prevalence of human papillomavirus infection in Mexican males: Comparative study of penile-urethral swabs and urine samples. *Sexually Transmitted Diseases, 28*(5), 277-280. https://doi.org/10.1097/00007435-200105000-00007

Le, V. N., Le, V. N. B., Hoang, X. S., & Le, V. D. (2024). Distribution of human papillomavirus among Vietnamese women with cervical cancer and unusual genetic variability of HPV16. *Virology, 594*, 110058. https://doi.org/10.1016/j.virol.2024.110058

Lineros-Hurtado, J. A., Romero, P., Salgado, Y. M., & Wiesner, C. (2020). Características operativas de técnicas moleculares empleadas para la detección del virus del papiloma humano en el proyecto ESTAMPA. *Revista Colombiana de Cancerología, 24*(3), 135-140. https://doi.org/10.35509/01239015.106

Liu, S., Mei, B., Ouyang, Y., & Li, C. (2023). Prevalence and genotype distribution of human papillomavirus infection among women in Jingzhou, China: A population-based study of 51,720 women. *Virology Journal, 20*(1), 297. https://doi.org/10.1186/s12985-023-02262-1

Minchalo, D. J., Oleas, H. L., & Bigoni, G. D. (2020). Prevalencia de los Genotipos del Virus del Papiloma Humano en mujeres de 25 a 65 años: Artículo Original. *Oncología (Ecuador), 30*(1), 39-52. https://doi.org/10.33821/471

Mogrovejo, A. R., Abad, J. N., Rivas, A. L., & Velecela, J. A. (2024). Virus del papiloma humano (VPH). En D. M. Caichug Rivera, *Infectología Clínica: Tomo II* (Primera). Puerto Madero Editorial. https://doi.org/10.55204/pmea.80.c180

Mojarrad, S., Najmafshar, M., Jahromi, Z. K., Salahi Ardekani, O., Shahraki, H. R., Jalvand, M., & Sana, F. A. (2025). Prevalence and genotype distribution of human papillomavirus in individuals referred to a laboratory in Urmia, Iran. *Infectious Agents and Cancer, 20*, 13. https://doi.org/10.1186/s13027-025-00636-4

Mosquera-Yuqui, F., Larrea, D., Ramos, O., Luna, B., García, M. F., Rojas, T., Silva, S., & Di

Stefano, M. (2025). Epidemiology of high-risk human papillomavirus among women of the north-central region of Ecuador: A retrospective study. *Infectious Agents and Cancer, 20*, 73. https://doi.org/10.1186/s13027-025-00700-z

Muñoz, N., Bosch, F. X., Sanjosé, S. de, Herrero, R., Castellsagué, X., Shah, K. V., Snijders, P. J. F., & Meijer, C. J. L. M. (2003). Epidemiologic Classification of Human Papillomavirus Types Associated with Cervical Cancer. *New England Journal of Medicine, 348*(6), 518-527. https://doi.org/10.1056/NEJMoa021641

Nagar, S. D., Conley, A. B., Chande, A. T., Rishishwar, L., Sharma, S., Mariño-Ramírez, L., Aguinaga-Romero, G., González-Andrade, F., & Jordan, I. K. (2021). Genetic ancestry and ethnic identity in Ecuador. *Human Genetics and Genomics Advances*, *2*(4), 100050. https://doi.org/10.1016/j.xhgg.2021.100050

Osmani, V., Hörner, L., Nkurunziza, T., Rank, S., Tanaka, L. F., & Klug, S. J. (2025). Global prevalence of cervical human papillomavirus in women aged 50 years and older with normal cytology: A systematic review and meta-analysis. *The Lancet Microbe*, *6*(1). https://doi.org/10.1016/j.lanmic.2024.100955

Osmani, V., Rossiter, M., Hörner, L., Nkurunziza, T., Rank, S., Tanaka, L. F., & Klug, S. J. (2025). Worldwide burden of cervical human papillomavirus (HPV) in women over 50 years with abnormal cytology: A systematic review and meta-analysis. *BMJ Global Health*, *10*(4). https://doi.org/10.1136/bmjgh-2024-017309

Pangarkar, M. A. (2022). The Bethesda System for reporting cervical cytology. *CytoJournal*, *19*, 28. https://doi.org/10.25259/CMAS_03_07_2021

Perkins, R. B., Guido, R. S., Castle, P. E., Chelmow, D., Einstein, M. H., Garcia, F., Huh, W. K., Kim, J. J., Moscicki, A. B., Nayar, R., Saraiya, M., Sawaya, G. F., Wentzensen, N., Schiffman, M., & 2019 ASCCP Risk-Based Management Consensus Guidelines Committee. (2020). 2019 ASCCP Risk-Based Management Consensus Guidelines for Abnormal Cervical Cancer Screening Tests and Cancer Precursors. *Journal of Lower Genital Tract Disease*, *24*(2), 102-131. https://doi.org/10.1097/LGT.0000000000000525

Rivera, A., Piedrahíta, P., Sánchez, E., Moreno, A., Espinosa, M., Arreaga, C., España, K., Parrales, E., Zhingre, A., Sánchez, S., Campoverde, A., Dalgo, P., Arévalo, P., Mendoza, M., Ruiz, J., Sánchez, M., Medina, L., Ibarra, A., Quimís, M., & Vega, P. (2018). Estudios

sobre el virus del papiloma humano (VPH) en el Ecuador, parte I. *Revista Científica Digital INSPILIP*, *2*(1), 1-22. https://doi.org/10.31790/inspilip.v2i1.39.g44

Rodriguez, L. K., Galárraga, R. I., Cabezas, J. C., Giler, J. R., Béjar, D. E., & Giler, É. P. (2006). Detección molecular y genotipificación del virus del papiloma humano en el Instituto Oncológico Nacional ION-SOLCA del Ecuador. *Medicina*, *11*(2), 114-117.

Solis-Ponce, L., Stosic, M., Curicó, G., Espetia, S., Sanchez-Grandez, H., Hassan, S. S., Basiletti, J., Søreng, K., Acuña-Barrios, M., Huarca-Balbin, L., Yaya-Ríos, M., Vilcarino-Zevallos, G., Lopez, R., Matos, A., Ramal-Asayag, C., Obregon, G., & Arroyo Mühr, L. S. (2025). Genotype distribution and molecular characterization of HPV in the Peruvian amazon: Insights into prevalence, lineage diversity, and viral integration. *Scientific Reports*, *15*(1), 32535. https://doi.org/10.1038/s41598-025-18455-3

Trujillo, T. C., Domínguez, S. R., Ríos, M. A., & Hernández, M. (2017). Prevalencia del virus del papiloma humano en mujeres con citología negativa. *Revista Cubana de Obstetricia y Ginecología*, *43*(1), 0-0.

Vives, A., Cosentino, M., & Palou, J. (2020). Evaluación del virus del papiloma humano en varones: Primera revisión exhaustiva de la literatura. *Actas Urológicas Españolas*, *44*(2), 86-93. https://doi.org/10.1016/j.acuro.2019.08.010

World Health Organization (WHO). (2021). *WHO guideline for screening and treatment of cervical pre-cancer lesions for cervical cancer prevention* (2nd ed.). Retrieved December 28, 2025, from https://www.who.int/publications/i/item/9789240030824

World Health Organization (WHO). (2024). *Human papillomavirus and cancer*. Retrieved December 28, 2025, from https://www.who.int/news-room/fact-sheets/detail/human-papilloma-virus-and-cancer

Zhou, Y., Barlogie, B., & Shaughnessy, J. D. (2009). The molecular characterization and clinical management of multiple myeloma in the post-genome era. *Leukemia*, *23*(11), 1941-1956. https://doi.org/10.1038/leu.2009.160

Zhu, L., Li, P., Wang, Y., Zhang, S., Xu, H., Zhang, J., Chen, J., Ren, J., Wu, Y., Yao, Y., Hua, Y., Li, P., Liu, Q., & Dan, L. (2025). The relationship between human papillomavirus genotype distribution and age and the association with high-grade squamous intraepithelial lesions of the cervix or cervical cancer in Jilin Province, China. *Virology Journal*, *22*(1), 380. https://doi.org/10.1186/s12985-025-02963-9

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